FORM PTO-1449	ATTY. DOCKET NO.	SERIAL NO.
LIST OF PATENTS AND OTHER ITEMS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	30727.0013.CIP1	09/518,501
	APPLICANT: METABASIS THERAPEUTICS, INC.	
	FILING DATE: March 5, 1999	GROUP: 1614

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE
	AA	3,018,302	01.23.62	Bielefeld, et al.			
	AB	5,157,027	10/20 92	Biller, et al.			
	AC	5,658,889	8/19/97	Gruber, et al.			

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION YES	TRANSLATION NO
	AD	0 002 062 A	30.05.79	EP (Abstract)				
	AE	0 072 531 A	23.02.83	EP (Abstract)				
	AF	0 158 057 A	16.10.85	EP (Abstract)				
	AG	0 180 276	28.12.88	EP				
	AH	0 261 283	22.09.86	EP				
	AI	0 161 955 A	21.11.85	EPO				
	AJ	0 338 372 A	25.10.89	EPO				
	AK	0 353 692 A	07.02.90	EPO				
	AL	0 481 214 A	22.04.92	EPO				
	AM	492 738 A	30.06.70	CH				
	AN	16 93 219 A	17.09.70	DE (Abstract)				

EXAMINER:	DATE CONSIDERED: 7/9/02

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FORM PTO-1449	ATTY. DOCKET NO.	SERIAL NO.
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(Use several sheets if necessary)	APPLICANT: METABASIS THERAPEUTICS, INC.	
	FILING DATE: March 5, 1999	GROUP: 1614

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION YES	TRANSLATION NO
	AO	35 12 781 A1	10.04.85	DE (and English language U.S. Patent No. 4,952,740)				
	AP	96/01267 A	18.01.96	WO				
	AQ	97/03679 A	06.02.97	WO				
	AR	98/09668 A	12.03.98	WO				
	AS	98/39342	11.09.98	WO				
	AT	98/39343	11.09.98	WO				
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

	AV	"Patent Abstracts of Japan," Vol. 1998, No. 1, 30 January 1998 & JP 09 241284 A (Yamishata Koji; Nippon Soda Co. Ltd), 16 September 1997
	AW	DeLombaert, et al., "*N*-Phosphonomethyl Dipeptides and Their Phosphonate Prodrugs, a New Generation of Neutral Endoprptidase (NEP, EC 3.4.24.11) Inhibitors, J. Med. Chem. 37: 498-511 (1994)
	AX	Edmunson, et al., "Cyclic Organophosphorus Compounds. Part 23. Configurational Assignments in the 4-Phenyl-1,3,2λ5-dioxaphosphorinane Series. X-Ray Molecular Structure of *cis*-2-Benzylamino-4-phenyl-1,3,2-dioxaphosphorinane 2-Oxide," J. Chem. Res. Synop., 5: 122-123 (1989)
	AY	Farquhar, et al., "5'-'4-(Pivaloyloxy)-1, 3, 2-dioxaphosphorin an –2-y]!-2'-deoxy-5-fluorouridine: a membrane-permeating prodrug of 5-fluoro-2'-deoxyuridylic acid (FDUMP)'" J. Med. Chem. 38:488-495 (1995)
	AZ	Farquhar, et al., "Biologically Reversible Phosphate-Protective Groups," J. Pharm. Sci. 72(3): 324 (1983)

all documents

EXAMINER: Examiner	DATE CONSIDERED: 2/4/02

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FORM PTO-1449	ATTY. DOCKET NO.	SERIAL NO.
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	APPLICANT: METABASIS THERAPEUTICS, INC.	
(Use several sheets if necessary)	FILING DATE: March 5, 1999	GROUP: 1614

OIPE JC1600 JUN 11 2001 PATENT & TRADEMARK OFFICE

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)		
	BA	Farquhar, et al., "Synthesis and Biological Evaluation of 9-[5'-(2-Oxo-1,3,2-oxazaphosphorinan-2-yl)-ß-D-arabinosyl]adenine and 9-[5'-(2-Oxo-1,3,2-dioxazaphosphorinan-2-yl)-ß-D-arabinosyl]adenine: Potential Neutral Precursors of 9-[ß-D-Arabinofuranosyl]adenine 5'-Monophosphate," J. Med. Chem. 28: 1358-1361 (1985)
	BB	Farquhar, et al., "Synthesis and Biological Evaluation of Neutral Derivatives of 5-Fluoro-2'-deoxyuridine 5'-Phosphate," J. Med. Chem. 26: 1153-1158 (1983)
	BC	Freed, et al., "Evidence For Acyloxymethyl Esters of Pyrimidine 5'-Deoxyribonucleotides as Extracellular Sources of Active 5'-Deoxyribonucleotides in Cultured Cells," Biochem. Pharmac. 38: 3193-3198 (1989)
	BD	Hillers, et al., "Analogs of pyrimidinemono-and polynucleotides. IV. Phosphates of 1-(1,4-dihydroxy-2-pentyl)thymine and 1-(1,3-dihydroxy-2-propyl) uracil." Khim Geterotski Soedin 5:678-683 (1978). Chem Abst. v 89 no 17; abst no 146864a
	BE	Hunston, et al., "Synthesis and Biological Properties of Some Cyclic Phosphotriesters Derived from 2'-Deoxy-5-fluorouridine," J. Med. Chem. 27: 440-444 (1984)
	BF	Kryuchkov, et al., Izv. Akad. Nauk SSSR, Ser. Khim. 6: 1201-1248 (1987)
	BG	Lok, et al., "Neurotoxicity associated with adenine arabinoside monophosphate in the treatment of chronic hepatitis B virus infection," J. Antimicrob. Chemotherap. 14: 93-99 (1984)
	BH	Ludeman, et al., "Synthesis and Antitumor Activity of Cyclophosphamide Analogues. 4. Preparation, Kinetic Studies, and Anticancer Screening of "Phenyl ketophos phamide" and Similar Compounds Related to the Cyclophosphamide Metabolyte Aldophosphamide," J. Med Chem. 29, 716-727 (1986)
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	BJ	Meyer, et al., "2"-O'-Acyl-6-thioinosine Cyclic 3', 5'-Phosphates as Prodrugs of Thioinosinic Acid," J. Med. Chem. 22: 811-815 (1979)
	BK	Neidlein, et al., "Mild Preparation of 1-Benzyloxyiminoalkylphosphonic Dichlorides: Application to the Synthesis of Cyclic Phosphonic Deisters and Cyclic Monoester Amides," Heterocycles 35: 1185-1203 (1993)

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	APPLICANT: METABASIS THERAPEUTICS, INC.	
(Use several sheets if necessary)	FILING DATE: March 5, 1999	GROUP: 1614

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)		
	BL	Nifant'ev, et al., "1,3,2, - Diazaphodsphorinanes", Zh. Obshch. Khim., Vol. 49, No. 1, 1979, Pages 64-74 (and English version as translated in corresponding English language publication)
	BM	Nifantyev, et al.,"Synthesis and Structure of Some Stable Phospholane-Phospholanes," Phos. Sulfur & Silicon 113, 1-13 (1996)
	BN	Predvoditelev D. , et al., "Glycero-2-hydroxymethylene phosphates" Journal of Organic Chemistry of the USSR (English Translation 13:1489-1492 (1977))
	BO	Predvoditelev, D. et al., "Synthesis of lipids and their models on the basis of glycerol alkylene phosphites. V. Cyclic phosphatidylglycerol and phosphatidylhydroxyhomocholine" Journal of Organic Chemistry of the USSR (English Translation 17:1156-1165 (1981)
	BP	Shaw & Cundy, "Biological Screens of PMEA Prodrugs," Pharm. Res. 10 (Suppl) S24 (1993)
	BQ	Shih, et al., "Preparation and Structures of 2-Dimethylamino-4-phenyl-1,3,2-dioxaphosphorinane-2-oxides," Bull. Inst. Chem. Acad. Sin. 41: 9-16 (1994)
	BR	Starrett, et al., "Synthesis, Oral Bioavailability Determination, and *in Vitro* Evaluation of Prodrugs of the Antiviral Agent 9-[2-(Phosphonomethoxy)-ethyl]adenine (PMEA)," J. Med. Chem. 37: 1957-1864 (1994)
	BS	Yamanaka, et al., "Metabolic Studies on BMS-200475, a New Antiviral Comound Active against Hepatitis B Virus," Antimicrob. Agents Chemoth. 43, 190-193 (1999)
	BT	Zon, et al., "4 Cyclophosphamide Analogues," Prog. Med. Chem. 19: 205-246 (1982)

All duplicates

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FORM PTO-1449	ATTY. DOCKET NO.	SERIAL NO.
LIST OF PATENTS AND OTHER ITEMS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	30727.001[illegible]IP1	09/518,501
#11 (Use several sheets if necessary)	APPLICANT: METABASIS THERAPEUTICS, INC.	
	FILING DATE: March 5, 1999	GROUP: 1[illegible]

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE
TCM	AA	3,018,302	01/23/62	Bielefeld, et al.	260	46[illegible]	—
TCM	AB	5,157,027	10/20/92	Biller, et al.	514	167	—
TCM	AC	5,658,889	8/19/97	Gruber, et al.	514	43	—

FOREIGN PATENT DOCUMENTS

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TCM	AD	0 002 062 A1	30.05.79	EP ~~(and English language Abstract)~~				
TCM	AE	0 072 531 A1	23.02.83	EP ~~(and English language Abstract)~~				
TCM	AF	0 158 057 A	16.10.85	EP (U.K. English language translation)				
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	AL	0 481 214 B1	22.04.92	EPO				
	AM	492 738	30.06.70	CH (and English language Abstract)				
	AN	987,378	17.09.70	UK				

EXAMINER:	DATE CONSIDERED:
[illegible]	7/8/02

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	APPLICANT: METABASIS THERAPEUTICS, INC.	
(Use several sheets if necessary)	FILING DATE: March 5, 1999	GROUP: 1614

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	AQ	97/03679	06.02.97	WO				
	AR	98/09668	12.03.98	WO				
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	AY	Farquhar, et al., "5'-'4-(Pivaloyloxy)-1, 3, 2-dioxaphosphorin an –2-y]l-2'-deoxy-5-fluorouridine: a membrane-permeating prodrug of 5-fluoro-2'-deoxyuridylic acid (FDUMP)'" J. Med. Chem. 38:488-495 (1995)
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FORM PTO-1449 LIST OF PATENTS AND OTHER ITEMS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	ATTY. DOCKET NO. 30727.001[redacted]IP1	SERIAL NO. 09/518,501
	APPLICANT: METABASIS THERAPEUTICS, INC.	
	FILING DATE: March 5, 1999	GROUP: 1614 1600

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)		
	BA	Farquhar, et al., "Synthesis and Biological Evaluation of 9-[5'-(2-Oxo-1,3,2-oxazaphosphorinan-2-yl)-ß-D-arabinosyl]adenine and 9-[5'-(2-Oxo-1,3,2-dioxazaphosphorinan-2-yl)-ß-D-arabinosyl]adenine: Potential Neutral Precursors of 9-[ß-D-Arabinofuranosyl]adenine 5'-Monophosphate," J. Med. Chem. 28: 1358-1361 (1985)
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	BL	Nifant'ev, et al., "1,3,2, - Diazaphodsphorinanes", Zh. Obshch. Khim., Vol. 49, No. 1979, Pages 53-61.
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 2

Complete if Known	
Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erion
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	030727.0013.CIP1

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U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	AA	Coppi, et al., "Lewis Acid Mediated Condensation of Alkenols and Aldehydes. A Selective Synthesis of Tetrahydropyrans and Oxepanes," J. Org. Chem., Vol. 53, No. 4, 911-913 (1988)	
	AB	Lohr et al., "Targeted chemotherapy by intratumor injection of encapsulated cells engineered to produce CYP2B1, and ifosfamide activating cytochrome P450," Gene Therapy, 5, 1070-1078 (1988).	
	AC	Bijsterbosch, et al., "Disposition of the Acyclic Nucleoside Phsophonate (S)-9-(3-Hydroxy-2-Phosphonylmethoxypropyl)Adenine," Antimicrobial Agents and Chemotherapy ," Vol. 42, p. 1146-1150 (May 1998).	
	AD	de Waziers, et al., "Cytochrome P 450 Isoenzymes, Epoxide Hydrolase and Glutathione Transferases in Rat and Human Hepatic and Extrahepatic Tissues1," The Journal of Pharmacology and Experimental Therapeutics, Vol. 253, No.1, p. 387-394 (1989).	

Examiner Signature		Date Considered	2/12/03

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation is not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 2 of 2

Complete if Known	
Application Number	09/518,501
Filing Date	March 5, 1999
First Named Inventor	Erion
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	030727.0013.CIP1

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
TM	AE	He, et al., "Inactivation of Cytochrome P450 3A4 by Bergamottin a Component of Grapefruit Juice," Chem. Res. Toxicol, Vol. 11, No. 4, p. 252-259 (1998).	
TM	AF	Jounaidi et al., "Retroviral Transfer of Human Cytochrome P450 Genes for Oxazaphosphorine-based Cancer Gene Therapy," Cancer Research, Vol. 58, p. 4391- 4401 (Oct. 1, 1998).	

Examiner Signature		Date Considered	2/13/03

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[1] Unique citation designation number. [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

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Sheet 1 of 1

Complete if Known	
Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erion et al.
Group Art Unit	1624
Examiner Name	McKenzie, T.
Attorney Docket Number	45198.00013.RCE (CIP1)

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
TM		6,054,587		Reddy et al.	04/25/00	
		6,110,903		Kasibhatla et al.	08/29/00	
		6,284,748		Dang et al.	09/04/01	
		6,294,672		Reddy et al.	09/25/01	
		6,312,662		Erion et al.	11/06/01	
		6,399,782		Kasibhatla et al.	06/04/02	
		6,489,476		Dang et al.	12/03/02	

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Examiner Signature	Tom McKenzie	Date Considered	4/16/04

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 1

Complete if Known	
Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erion et al.
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	45198.00013.RCE

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		FARQUHAR et al., "Synthesis and Antitumor Evaluation of Bis[pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," J. Med. Chem., 37:3902-3909 (1994).	
		LEFEBVRE, et al., Mononucleotide Phosphotriester Derivatives with S-Acyl-2-thioethyl Bioreversible Phosphate-Protecting Groups: Intracellular Delivery of 3'-Azido-2',3'-dideoxythymidine 5'-Monophosphate," J. Med. Chem., 38:3941-3950 (1995).	

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Sheet 1 of 3

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Attorney Docket Number	032465.00013.RCE (CIP1)

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		Beaucage and Iyer, "The Synthesis of Modified Oligonucleotides by the Phosphoramidite Approach and Their Applications," Tetrahedron, 49(28):6123-6194 (1993).	
		Borch and Millard, "The Mechanism of Activation of 4-Hydroxycyclophosphamide," J. Med. Chem., 30:427-431 (1987).	
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Sheet 2 of 3

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Group Art Unit	1624
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Examiner Signature	Tom McKenzie	Date Considered	4/16/07

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